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(54) Title: PROTECTIVE ANTIGENS FOR THE CONTROL OF IXODES SPECIES INFESTATIONS

(57) Abstract: Protective antigens against infestations with *Ixodes* spp. ticks, gene sequences and encoded proteins for such antigens, related vaccines and methods useful to induce an immune response, which are protective to interfere with infestations by *Ixodes* spp. ticks.

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PROTECTIVE ANTIGENS FOR THE CONTROL OF *IXODES* SPECIES INFESTATIONS

BACKGROUND OF THE INVENTION

Technical Field:

The present invention relates to the identification of protective antigens against infestations with *Ixodes* spp. ticks, gene sequences and encoded proteins for such antigens, related vaccines and methods useful to induce an immune response, which are protective to interfere with infestations by *Ixodes* spp. ticks.

Background:

Ticks parasitize wild, domesticated animals and humans and transmit pathogens including fungi, bacteria, viruses and protozoon. Currently, ticks are considered to be second in the world to mosquitoes as vectors of human diseases, but they are considered to be the most important vector of pathogens in North America (Parola and Raoult, 2001). *Ixodes spp.* are distributed worldwide and act as vectors of human diseases caused by *Borrelia burgdorferi* (Lyme disease), *Anaplasma phagocytophila* (human granulocytic ehrlichiosis), *Coxiella burnetti* (Q fever), *Francisella tularensis* (tularemia), *B. afzelii*, *B. lusitaniae*, *B. valaisiana* and *B. garinii*, *Rickettsia helvetica*, *R. japonica* and *R. australis*, *Babesia divergens* and tick-borne encephalitis (TBE) and Omsk Hemorrhagic fever viruses (Estrada-Peña and Jongejan, 1999; Parola and Raoult, 2001). Throughout eastern and southeastern United States and Canada, *I. scapularis* (the black legged tick) is the main vector of *B. burgdorferi* sensu stricto and *A. phagocytophila* (Estrada-Peña and Jongejan, 1999; Parola and Raoult, 2001).

Control of tick infestations is difficult and often impractical for multi-host ticks such as *Ixodes* spp. Presently, tick control is effected by integrated pest management in which different control methods are adapted to one area or against one tick species with due consideration to their environmental effects. Recently, development of vaccines against one-host *Boophilus spp.* has provided new possibilities for the identification of protective antigens for immunization against tick infestations (Willadsen, 1997; Willadsen and Jongejan, 1999; de la Fuente et al., 1999; 2000; de Vos et al., 2001). The recombinant *B. microplus* BM86 gut antigen included in commercial vaccine formulations TickGARD (Hoechst Animal Health, Australia) and Gavac (Heber Biotec S. A., Havana, Cuba) also confers partial protection against phylogenetically related *Hyalomma* and *Rhipicephalus* tick genera (de la Fuente et al., 2000; de Vos et al., 2001). However, immunization with BM86 failed to protect against the more phylogenetically distant *Amblyomma* spp. (de Vos et al., 2001). These results suggest that using Bm86 or a closely related gene for the production of vaccines against *Ixodes* spp. or other tick genera phylogenetically distant from *Boophilus* spp. (Black and Piesman, 1994) could be impractical. Therefore, the screening for novel protective antigens is necessary to identify vaccine candidates against infestations with these tick species of medical and veterinary importance. Control of ticks by vaccination would avoid environmental contamination and selection of drug resistant ticks that result from repeated acaricide application (de la Fuente et al., 1998; Garcia-Garcia et al., 1999). Anti-tick vaccines also allow for inclusion of multiple antigens in order to target a broad range of tick species and for incorporation of pathogen-blocking antigens.

Vaccination with DNA and cDNA molecules has been used to induce a protective immune response against *B. microplus* and several pathogens in laboratory

animals and livestock (De Rose et al., 1999; Drew et al., 1999; van Drunen Littel-van den Hurk et al., 2001; Kofta and Wedrychowicz, 2001). A new technique, expression library immunization (ELI) in combination with sequence analysis provides an alternative approach for identification of potential vaccine antigens based on rapid screening of the expressed genes without prior knowledge of the antigens encoded by cDNA clones. ELI was first reported for *Mycoplasma pulmonis* (Barry et al., 1995) and since then has been used for unicellular and multicellular pathogens and viruses (Manoutcharian et al., 1998; Alberti et al., 1998; Brayton et al., 1998; Melby et al., 2000; Smooker et al., 2000; Moore et al., 2002; Singh et al., 2002). However, the identification of individual protective clones has not been reported and it is predicted that identification of protective antigens will be more difficult as the complexity of the genome increases.

Although several reports in the literature have demonstrated by ELI that libraries can offer a degree of protection (Barry et al., 1995; Manoutcharian et al., 1998; Alberti et al., 1998; Brayton et al., 1998; Melby et al., 2000; Smooker et al., 2000; Moore et al., 2002; Singh et al., 2002), none have applied ELI to arthropods and particularly to ticks. Several vaccines have been developed to protect humans against *Ixodes*-transmitted pathogens including TBE virus and *B. burgdorferi*. However, it is not clear whether these vaccines will protect against all pathogen strains and genotypes. The inclusion of tick immunogens in pathogen-specific vaccines could enhance their protective effect and increase efficacy (Nuttall, 1999). This transmission-blocking approach is supported by evidence that host resistance to ticks provides some protection against tick-borne transmission of viruses and *B. burgdorferi* (Wikel et al., 1997). Furthermore, vaccination against *B. microplus* has

been demonstrated to contribute to the control of tick-borne diseases (de la Fuente et al., 1998; 1999).

SUMMARY OF THE INVENTION

The present invention is based upon our identification by ELI and sequence analysis of protective cDNA clones against experimental infestations with *I. scapularis*. This is the first example of the application of ELI to arthropods and particularly to ticks. The protective antigens are homologous to endopeptidases, nucleotidases, chorion proteins, vitellogenin receptors, peptidoglycan recognition proteins, glutamine-alanine rich proteins, ribosomal proteins, ß-adaptin, Beta-amyloid precursor protein, Block of proliferation (Bop1), lectins, chloride channels, RNA polymerases, ATPases and heat-shock proteins. These antigens induce an immune response in vaccinated hosts that either interferes with tick development or results in a pro-feeding activity, which could be due to the expression of cDNAs encoding for tick immunosuppressants, anticoagulants and other proteins with low antigenicity and a pro-feeding activity or they could encode for proteins homologous to host proteins with anti-tick activity, which neutralization results in a tick pro-feeding activity. These protective antigens, although identified for *I. scapularis*, may be cross protective between *Ixodes* species considering the high degree of conservation of gene sequences and protein function between species of the same genus. A 5'-nucleotidase was identified and characterized in *B. microplus* by Liyou et al. (1999; 2000) but they did not assay its protection capacity. Although surprising at first glance, the protection capacity of ribosomal and heat shock protein preparations has been previously documented in other organisms (Elad and Segal, 1995; Silva, 1999; Melby et al., 2000; Cassataro et al., 2002) but never in ticks. The effect of cDNA vaccination on *I. scapularis*

experimental infestations of mice was evidenced by the reduction of the number of engorged larvae, the retardation of larval development, the inhibition of molting to nymphal stages and the appearance of visibly damaged larvae with red coloration. These effects were also recorded in vaccination experiments with recombinant BM86 and BM95 against infestations with *B. microplus*, including the red coloration in some ticks, attributed to blood leakage to the tick haemolymph (Garcia-Garcia et al., 2000).

Thus, in one embodiment of the present invention there is provided cDNA sequences, protein encoding fragments thereof, and derived protein sequences for protective *I. scapularis* antigens comprising antigens homologous to endopeptidases, nucleotidases, chorion proteins, vitellogenin receptors, peptidoglycan recognition proteins, glutamine-alanine rich proteins, ribosomal proteins, ß-adaptin, Beta-amyloid precursor protein, Block of proliferation (Bop1), lectins, chloride channels, RNA polymerases, ATPases and heat-shock proteins.

In another embodiment of the present invention there is provided a vaccine composition comprising the *I. scapularis* protective recombinant proteins and/or modified cDNAs separately or which may optionally be combined with adjuvant to enhance the protection efficacy of vaccine preparations against *Ixodes* spp., wherein the vaccine composition further comprises a pharmaceutically acceptable carrier or diluent. The vaccine composition also may optionally be combined with tick-borne pathogen components to provide a means to control tick-borne infections, wherein the vaccine composition further comprises a pharmaceutically acceptable carrier or diluent and adjuvant.

In another embodiment of the present invention there is provided a method for inducing an immune response in a mammal to provide immune protection, which reduces or affects infestations by *Ixodes* spp. ticks and/or transmission of tick-borne

pathogens, the method comprising administering to at-risk human population and mammalian reservoir an effective amount of a vaccine composition comprising the *I. scapularis* protective recombinant proteins and/or modified cDNAs alone or in combination with an adjuvant or tick-borne pathogen components to provide a means to control tick infestations and to reduce transmission to humans of tick-borne infections, wherein the vaccine composition further comprises a pharmaceutically acceptable carrier or diluent.

A better understanding of the present invention and its objects and advantages will become apparent to those skilled in this art from the following detailed description, wherein there is described only the preferred embodiment of the invention, simply by way of illustration of the best mode contemplated for carrying out the invention. As will be realized, the invention is capable of modifications in various obvious respects, all without departing from the scope and spirit of the invention. Accordingly, the description should be regarded as illustrative in nature and not as restrictive.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG 1 is a summary of the cDNA ELI approach used to identify protective antigens against *I. scapularis* infestations.

FIG. 2A is a graph depicting the results of a primary screen of cDNA pools (A-H 1-4, A5) by ELI. V, control mice injected with 1 μg vector DNA alone. *α<0.01, **α<0.05 (Tukey's *post-hoc* test for pair comparisons after ANOVA). Number in boxes represent values for inhibition of tick infestation with respect to the control group.

FIG. 2B is a graph depicting the results of a primary screen of cDNA pools (A6-A10, B-H 5-8) by ELI. V, control mice injected with 1 μg vector DNA alone. *α<0.01, **α<0.05 (Tukey's *post-hoc* test for pair comparisons after ANOVA). Number in boxes represent values for inhibition of tick infestation with respect to the control group.

FIG. 3 is a graph depicting the results of a tertiary screen by ELI of cDNA sub-pools formed according to the predicted function of encoded proteins. Only groups with I≥15% are shown (white bars). The number of engorged larvae per mouse is expressed as mean±SD (black bars). Control mice were injected with mitochondrial (MT) cDNAs. *P≤0.05 (Student's t-test).

DETAILED DESCRIPTION OF THE INVENTION

Before explaining the present invention in detail, it is important to understand that the invention is not limited in its application to the details of the construction illustrated and the steps described herein. The invention is capable of other embodiments and of being practiced or carried out in a variety of ways. It is to be understood that the phraseology and terminology employed herein is for the purpose of description and not of limitation.

The present invention derives from the sequences set forth on the Sequence Listing attached hereto and incorporated herein. In particular, there is provided 25 separate and distinct sequences comprising 14 cloned cDNA molecules and 11 deduced amino acid sequences of encoded polypeptides, said sequences having been isolated and identified as possessing the asserted utility in accordance with the following described experimental methodology.

Example 1: Construction of an I. scapularis cDNA library and screening for protective antigens by ELI

Tick cells

Monolayers of IDE8 (ATCC CRL 1973) cells, originally derived from embryonic *I. scapularis*, were maintained at 31°C in L-15B medium supplemented with 5% foetal bovine serum, tryptose phosphate broth and bovine lipoprotein concentrate after Munderloh et al. (1994). Cells were subcultured at 1:5 – 1:10 when monolayers reached a density of approximately 10^7 cells/T-25 flask. Medium was replaced weekly.

Library construction

A cDNA expression library was constructed in the vector pEXP1 containing the strong cytomegalovirus CMV_{IE} promoter (Clontech). Because we planned to target the early larval stages of *I. scapularis*, we chose to construct our library from cultured embryonic *I. scapularis* IDE8 cells-derived poly(A)+ RNA. The cDNA library contained 4.4 x 10^6 independent clones and a titer of approximately 10^{10} cfu/ml with more than 93% of the clones with cDNA inserts. The average cDNA size was 1.7 kb (0.5-4.0 kb).

Primary screen

The overall schema for identification of protective antigens through ELI, sequential fractionation and sequence analysis is shown in Fig. 1.

Ninety-six LBA (master) plates containing an average of 41 (30-61) cDNA clones per plate were prepared. Replicas were made and clones from each plate were pooled, inoculated in Luria-Bertani with 50 µg/ml ampicillin, grown for 2 hr in a 96 wells plate and plasmid DNA purified from each pool (Wizard SV 96 plasmid DNA purification system, Promega, Madison, WI, USA). BALB/c female mice, 5-6 weeks of age at the time of first vaccination, were used. Mice were cared for in accordance

with standards set in the Guide for Care and Use of Laboratory Animals. Mice were injected with a 1 ml tuberculin syringe and a 27 gauge needle at days 0 and 14. Three mice per group were each immunized IM in the thigh with 1 μg DNA/dose in 50 μl PBS. Two groups of 3 mice each were included as controls. One group was injected with 1 μg vector DNA alone and the second with saline only. Two weeks after the last immunization, mice were infested with 100 *I. scapularis* larvae per mouse. Ticks were artificially reared at the Oklahoma State University tick rearing facility by feeding larvae on mice, nymphs on rabbits and adults on sheep and using for infestation in our experiments the larvae obtained from the eggs oviposited by a single female. Twelve hours after tick infestation, larvae that did not attach were counted to calculate the number of attached larvae per mouse and mice were transferred to new cages. Replete larvae dropping from each mouse were collected daily and counted during 7 days. The inhibition of tick infestation (I) for each test group was calculated with respect to vector-immunized controls as [1-(<RL>n/<RL>c x <RL>ic/<RL>in)] x 100, where <RL>n is the average number of replete larvae recovered per mouse for each test group, <RL>c is the average number of replete larvae recovered per mouse for control group, <RL>ic is the average number of larvae attached per mouse for control group, and <RL>in is the average number of larvae attached per mouse for each test group.

Pools of 41 (30-61) *I. scapularis* cDNA clones were screened by ELI. Only 33 cDNA pools and controls were analyzed per experiment. The average tick infestation level was 50±13 and 56±15 and 56±15 and 54±18 larvae/mouse for cDNA immunized and control mice, respectively ($P>0.05$) (Table 1). The average number of engorged larvae recovered per mouse was 9±3 and 13±4 in the cDNA-immunized mice and 16±4 and 17±3 in the control vector-immunized group ($P<0.05$) (Table 1).

No reduction was observed in the number of larvae collected from mice that received the vector DNA compared to saline-immunized controls. The maximum number of engorged larvae was collected 3 to 4 days after infestation. However, in mice immunized with cDNA pools B5, A8 and A10 (Fig. 2) a retardation of larval development in 1 to 2 days was recorded. The average inhibition of tick infestation (I) was 49±28% and 30±22% (Table 1). After two experiments covering the analysis of 66 pools (2705 clones), 9 protective pools (351 clones) were selected producing an inhibition of tick infestation I≥60% (Fig. 2A and 2B and Table 1). When we started these experiments, we planed to screen over 4000 cDNA clones considering the complexity of the tick genome. However, to our surprise 9 protective cDNA pools were identified after screening 66 pools containing 2705 cDNA clones. This result probably reflects the possibility of interfering with tick infestations at many different levels that involve a Pleiades of gene products. Results from vaccination experiments against ticks employing recombinant antigens support this view (reviewed by Mulenga et al., 2000). Because of the complexity of the screening procedure in mice vaccinated and challenged with tick larvae, it was difficult to work with more than 9 protective cDNA pools. Therefore we did not continue screening new cDNA pools and focused our attention on the 9 pools selected after the primary screen.

Secondary screen

The secondary screen was done to verify the protective capacity of the cDNA pools selected after the primary screen (Fig. 2A and 2B). After the primary screen of 66 cDNA pools (2705 clones), 9 pools with I≥60% were selected for the secondary screen (re-screening) employing 5 mice per group as described above. Engorged larvae were kept for molting in a 95% humidity atmosphere. Molting of engorged larvae was evaluated by visual examination of tick nymphs under a stereomicroscope

34 days after last larval collection. The inhibition of molting (M) for each test group was calculated with respect to vector-immunized controls as [1-(MLn/MLc x RLc/RLn)] x 100, where MLn is the number of nymphs for each test group, MLc is the number of nymphs for the control group, RLc is the number of larvae recovered for the control group, and RLi is the number of larvae recovered for each test group. Control mice were immunized with the negative (I=0%) F2 cDNA pool or saline only. A group was included immunized SC with two doses of 100 µg of total IDE8 tick cell proteins per dose in Freund's incomplete adjuvant.

All 9 protective cDNA pools gave positive results in the secondary screen (data not shown). The tick infestation levels were higher in this experiment (average 85±6 and 84±3 larvae/mouse for cDNA-immunized and control mice, respectively; $P>0.05$). Nevertheless, the average number of engorged larvae recovered per mouse was 39±7 and 26±6 for control and cDNA-immunized mice, respectively ($P<0.05$). The group immunized with total IDE8 tick cell proteins was protected with I=33%. Again, no reduction was observed in the number of larvae collected from mice that received the control cDNA (F2 negative pool after the primary screen; Fig. 2A) compared to saline-immunized controls.

In the secondary screen, molting of engorged larvae was evaluated after 34 days. Molting was affected in all but one test cDNA-immunized group. Inhibition of molting in test cDNA-immunized mice compared to the control cDNA-immunized group varied from 0% to 12% (6±4%). The inhibition of molting was higher than 50% only in the larvae collected from mice immunized with cDNA pools B5 and A10, which showed a retardation of larval development in 1 to 2 days as in the primary screen. No differences were observed between control cDNA and saline-immunized mice. Among the larvae that did not molt to nymph, some were visibly damaged and

presented a strong red coloration. The percent of red larvae in cDNA-immunized mice varied between 3% to 18 % (7±5%) while in the saline and control cDNA-immunized groups red larvae represented the 6% and 4%, respectively.

Tertiary screen

For the tertiary screen, 64 clones were grouped in 16 sub-pools each containing 1 to 17 plasmids according to the predicted function of encoded proteins (e.g., all the plasmids that encoded histone proteins were grouped together) and used with 4 sub-pools containing 182 clones of unknown function or with sequences without homology to sequence databases to immunize 4 mice per group. Mice were immunized with 0.3 µg/plasmid/dose in 50 µl PBS and evaluated as described above. Control mice were immunized with a pool of 20 plasmids containing mitochondrial cDNAs.

Tick infestation levels were similar in all test groups (72±2 larvae/mouse) and in control mice (69±2 larvae/mouse) ($P>0.05$). The number of engorged larvae recovered per mouse was also similar between test (16±7) and control (14±6) mice ($P>0.05$). However, the groups immunized with cDNA sub-pools containing clones with putative endopeptidase, nucleotidase, ribosomal proteins, heat shock proteins, glutamine-alanine-rich proteins and 3 of the sub-pools with unknown function or with sequences without homology to sequence databases had $I\geq 15\%$ (Fig. 3). Furthermore, among them, the groups immunized with sub-pools containing clones with a putative endopeptidase, nucleotidase and two of the cDNA sub-pools with unknown function or with sequences without homology to sequence databases resulted in lower infestation levels compared to control mice ($P\leq 0.05$) and $I\geq 40\%$ (Fig. 3). Clones homologous to chorion proteins, vitellogenin receptors, and peptidoglycan recognition

proteins were selected for they potential protection capacity in other stages of tick development.

Statistical analysis

The number of larvae attached per mouse and the number of engorged larvae recovered per mouse 7 days after infestation were compared by Analysis of Variance (ANOVA) followed by a series of Tukey's *post-hoc* tests for pair comparisons between cDNA-immunized and control vector DNA-immunized mice (primary screen), and by Student's t-test between mice immunized with positive cDNA pools and the control negative F2 cDNA pool (secondary screen) or between test cDNA sub-pools-immunized and control mice immunized with mitochondrial cDNAs (tertiary screen).

Example 2: Sequence analysis of protective clones

All the 351 cDNA clones in the 9 pools that resulted positive in the secondary screen were sequenced. DNA from individual clones in these pools was purified (Wizard SV 96 plasmid DNA purification system, Promega) from the master plate and partially sequenced. In most cases a sequence larger than 700 nucleotides was obtained. Nucleotide sequences were analyzed using the program AlignX (Vector NTI Suite V 5.5, InforMax, North Bethesda, MD, USA). BLAST (Altschul et al., 1990) was used to search the NCBI databases to identify previously cloned sequences that may have homology to those that we sequenced. Sequence analysis allowed grouping the clones according to sequence identity to DNA databases and predicted protein function. The protective clones selected after the tertiary screen were fully sequenced.

Comparison to sequence databases permitted to identify sequence identity to previously reported genes with known function in 152 (43%) of the clones (Table 2).

Fifty seven percent of the sequences were homologous to genes with unknown function or had no significant identity to previously reported sequences (Table 2). Of the clones with sequence identity to genes with known function, 85% were homologous to arthropod sequences. Ninety-three clones (61%) contained sequences homologous to *Drosophila melanogaster*, 5 (3%) to other insects and 32 (21%) to Ixodid tick species. Thirty percent of the clones were eliminated from further analysis based on their sequence identity, including those containing similar sequences (Table 2). The protective clones included antigens homologous to endopeptidases, nucleotidases, chorion proteins, vitellogenin receptors, peptidoglycan recognition proteins, glutamine-alanine rich proteins, ribosomal proteins, and heat-shock proteins.

Summary of results

The results obtained with the various protective clones identified in the Sequence Listing, along with certain selected expressed proteins, are summarized in Table 4.

SEQ ID NO:1 denotes the clone designated 4E6, wherein the relevant protein encoding fragment has been identified as comprising residues 1-117, which encodes the polypeptide shown in SEQ ID NO: 2.

SEQ ID NO:3 denotes the clone designated 4D8, wherein the relevant protein encoding fragment has been identified as comprising residues 80-575, which encodes the polypeptide shown in SEQ ID NO: 4.

SEQ ID NO:5 denotes the clone designated 4F8, wherein the relevant protein encoding fragment has been identified as comprising residues 1-951, which encodes the polypeptide shown in SEQ ID NO: 6.

SEQ ID NO:7 denotes the clone designated 4G11, wherein the relevant protein encoding fragment has been identified as comprising residues 1-697, which encodes the polypeptide shown in SEQ ID NO: 8.

SEQ ID NO:9 denotes the clone designated 4D6, wherein the relevant protein encoding fragment has been identified as comprising residues 198-1025, which encodes the polypeptide shown in SEQ ID NO: 10.

SEQ ID NO:11 denotes the clone designated 3E1, wherein the relevant protein encoding fragment has been identified as comprising residues 3-578, which encodes the polypeptide shown in SEQ ID NO: 12.

SEQ ID NO:13 denotes the clone designated 1C10, wherein the relevant protein encoding fragment has been identified as comprising residues 1-1119, which encodes the polypeptide shown in SEQ ID NO: 14.

SEQ ID NO:15 denotes the clone designated 3E10, wherein the relevant protein encoding fragment has been identified as comprising residues 51-1544, which encodes the polypeptide shown in SEQ ID NO: 16.

SEQ ID NO:17 denotes the clone designated 4F11, wherein the relevant protein encoding fragment has been identified as comprising residues 31-2295, which encodes the polypeptide shown in SEQ ID NO: 18.

SEQ ID NO:19 denotes the clone designated 3C12, wherein the relevant protein encoding fragment has been identified as comprising residues 6-332, which encodes the polypeptide shown in SEQ ID NO: 20.

SEQ ID NO:21 denotes the clone designated 2C12, wherein the relevant protein encoding fragment has been identified as comprising residues 3-137, which encodes the polypeptide shown in SEQ ID NO: 22.

SEQ ID NOS: 22, 23 AND 24, denote, respectively, clones 1A9, 1B2 and 4A4, each comprising a partial sequence with no associated polypeptide.

* * * * *

As noted above, the present invention relates to the sequences identified in the Sequence Listing. More generally, the invention concerns the given cDNA sequences and any nucleotide sequence coding for a protein which is capable of eliciting an antibody or other immune response (e.g., T-cell response of the immune system) which recognizes an epitope(s) of the amino acid sequences depicted in the Sequence Listing, including less than the full cDNA sequences and mutants thereof. Hence the nucleotide sequence may encode a protein which is the entire antigen encoded by the variously identified bases, or a fragment or derivative of the antigen or a fusion product of the antigen or fragment and another protein, provided that the protein which is produced from such sequence is capable of eliciting an antibody or other immune response which recognizes an epitope(s) of the given amino acid sequences.

As a result, the invention encompasses DNA sequences which encode for and/or express in appropriate transformed cells, proteins which may be the full length antigen, antigen fragment, antigen derivative or a fusion product of such antigen, antigen fragment or antigen derivative with another protein.

Proteins included within the present invention have an amino acid sequence depicted in the Sequence Listing. Other included proteins consist of a fragment of said sequence capable of eliciting an antibody or other immune response which recognizes an epitope(s) of the amino acid sequences depicted and a mutuant of said sequence capable of eliciting an antibody or other immune response which recognizes an epitope(s) of such amino acid sequences.

The nucleotide sequences may be inserted into any of a wide variety of expression vectors by a variety of procedures. Such procedures and others are deemed to be known by those skilled in the art. Suitable vectors include chromosomal, nonchromosomal and synthetic DNA sequences; e.g., derivatives of SV40; bacterial plasmids; phage DNAs; yeast plasmids; vectors derived from combinations of plasmids and phage DNAs, viral DNA such as baculovirus, vaccinia, adenovirus, fowl pox virus, pseudorabies, etc. The appropriate DNA sequence must be operatively linked in the vector to an appropriate expression control sequence(s) (promoter) to direct mRNA synthesis. As representative examples of such promoters, there may be mentioned LTR or SV40 promoter, the E. coli lac or trp, the phage lambda PL promoter and other promoters known to control expression of genes in prokaryotic and eukaryotic cells or their viruses. The expression vector also includes a non-coding sequence for a ribosome binding site for translation initiation and a transcription terminator. The vector may also include appropriate sequences for amplifying expression.

The vector containing the appropriate cDNA sequence as hereinabove described, as well as an appropriate promoter or control sequence, may be employed to transform an appropriate host to permit the host to express the protein. Examples of host organisms and cells include bacterial strains (e.g., *E. coli*, Pseudomonas, *Bacillus*, *Salmonella*, etc.), fungi (e.g., yeasts and other fungi), animal or plant hosts (e.g., mouse, swine or animal and human tissue cells). The selection of the host is deemed to be within the scope of those skilled in the art.

It is also understood that the appropriate cDNA sequence present in the vector when introduced into a host may express part or only a portion of the protein which is encoded within the noted terminology, it being sufficient that the expressed protein be

capable of eliciting an antibody or other immune response which recognizes an epitope(s) of the listed amino acid sequences.

The isolated cDNAs and/or polypeptide expressed by the host transformed by the vector may be harvested by methods which will occur to those skilled in the art and used in a vaccine for protection of a mammal, such as a bovine, swine, human, etc., against infestations of *Ixodes* species. Such protective recombinant proteins and/or modified cDNAs are used in an amount effective to induce an immune response against *Ixodes* species ticks and their associated pathogens and may be used in combination with a suitable physiologically acceptable carrier. The term "inducing an immune response" when used with respect to the vaccine described herein means that the vaccine prevents disease associated with a particular tick species or reduces the severity of the disease.

The carrier employed in conjunction with vaccine may be any one of a wide variety of carriers. As representative examples of suitable carriers, there may be mentioned mineral oil, synthetic polymers, etc. Carriers for vaccines are well known in the art and the selection of a suitable carrier is deemed to be within the scope of those skilled in the art. The selection of a suitable carrier is also dependent upon the manner in which the vaccine is to be administered.

The present invention provides a method of immunizing a susceptible mammal, against infestations and disease caused by *Ixodes* species with the vaccine described above. For purposes of this invention, the vaccine is administered in an effective amount. The vaccine may be administered by any of the methods well known to those skilled in the art, for example, by intramuscular, subcutaneous, intraperitoneal or intravenous injection. Alternatively, the vaccine may be administered intranasally or orally. It is also to be understood that the vaccine may

include active components, such as tick-borne pathogen components or adjuvants in addition to the antigen(s) or fragments hereinabove described.

The host expressing the antigen may itself be used to deliver antigen to non-human animals, by introducing killed or viable host cells that are capable of propagating in the animal. Direct incorporation of the cDNA sequences into host cells may also be used to introduce the sequences into animal cells for expression of antigen in vivo.

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Table 1. Primary screen of the *I. scapularis* cDNA library by ELI in mice.

Experimental group[a]	Number of pools screened (Number of clones)	Average±SD number of larvae attached per mouse[b]	Average±SD number of engorged larvae per mouse[c]	Average±SD inhibition of tick infestation (I)[d]	Number of pools selected for the secondary screen
Experiment 1	33 (1383)	50±13 (33-80)	9±3 (2-42)	39±55% (-183 - 87%)	6 (I>75%)
Vector DNA-immunized controls for experiment 1	—	56±13 (45-67)	16±4 (5-27)	—	—
Experiment 2	33 (1322)	56±15 (29-79)	13±4 (1-27)	27±28% (-53 - 89%)	3 (I>60%)
Vector DNA-immunized controls for experiment 2	—	54±18 (36-73)	17±3 (6-28)	—	—

[a]Ninety six LBA plates containing an average of 41 cDNA clones per plate were prepared. Replicas were made and clones from each plate were pooled, inoculated, grown for 2 hr in a 96 wells plate and plasmid DNA purified from each pool for ELI. Three mice per group were each immunized IM twice with 1 μg DNA/dose in 50 μl PBS two weeks apart. Two groups of 3 mice each were included as controls. One group was injected with vector DNA and the second with saline only.

[b]Fifteen days after the last immunization, mice were infested with 100 *I. scapularis* larvae per mouse. Twelve hrs later, larvae that did not attach were counted to calculate the number of attached larvae per mouse and mice were transferred to new cages.

[c]Engorged larvae dropping from each mouse were collected daily and counted after 7 days.

[d]The inhibition of tick infestation (I) for each test group was calculated with respect to vector-immunized controls as [1-(RLn/RLc x RLic/RLin)] x 100, where RLn is the average number of replete larvae recovered per mouse for each test group, RLc is the average number of replete larvae recovered per mouse for control group, RLic is the average number of larvae attached per mouse for control group, and RLin is the average number of larvae attached per mouse for each test group.

Table 2. Classification of the clones in protective pools by putative protein function according to identity to sequence databases.

Putative protein Function	Number of clones
Biosynthetic[a]	2
Catabolism	4
Cell adhesion	2
Cell cycle[a]	2
Cytoskeletal[a]	8
Defense	2
DNA structure or replication[a]	3
Extracellular matrix	3
Endocytosis	2
Energy metabolism	10
Homeostasis	2
Morphogenetic	9
Mitochondrial[a]	34
Protein synthesis or processing[a,b]	34
RNA synthesis or processing[a]	7
Heat-shock proteins	4
Signal transduction	16
Transport	8
Unknown	199
Total	351

[a]Eliminated from further screening of protective antigens. Other clones were eliminated for containing similar sequences.

[b]Except for ribosomal proteins.

Table 3. Grouping of the clones according to the predicted function of encoded proteins in sub-pools for the tertiary screen.

Sub-pool (No. of clones)	Clone	Pool[a]
Ribosomal (17)	1A2, 1A10, 1C11	A5
	1F6	D1
	2B8	A10
	2F8, 2F10	E8
	3A10, 2C3, 3D2, 3D10	B4
	3G9, 3G10	E3
	4D11, 4D12, 4E7, 4F7	F1
Membrane protein (7)	1D8, 1D11, 1E10	D1
	2B12	A10
	2H5	E8
	3C9	B4
	3G11	E3
ATPase (6)	1A9, 1B2, 1C9	A5
	2C9	A10
	4A4	C3
	4G12	F1
Cell channel/Transporter (5)	1F4	D1
	2H11	E8
	4A12	C3
	4G10, 4G11	F1
Early development-specific (4)	1C8	A5
	3F4	E3
	4C7	C3
	4G9	F1
G protein-coupled receptor (4)	2B7, 2C12	A10
	2F12	E8
	4C9	C3
Growth factor receptor (3)	2E8	B5
	3B8, 3C8	B4
Lectin (3)	3E10	E3
	4B8, 4C8	C3
Vitellogenin (3)	1F12	D1
	4A6	C3
	4G2	F1
Heat shock (3)	1C10	A5
	1F10	D1
	3F6	E3
EGF-like (2)	2H4	E8
	4C10	C3
Secreted protein (2)	2F9	E8
	3C12	B4
Glutamine-Alanine rich (2)	4D6, 4E6	F1
Adaptin (1)	3E1	E3
Endopeptidase (1)	4D8	F1
Nucleotidase (1)	4F8	F1

[a]cDNA pools refer to positive pools after primary and secondary screens (Fig. 2A and 2B).

Table 4: Summary of results with *I. scapularis* cDNA clones.

cDNA clone	Predicted Protein	Inhibition of tick infestation I (%)	Inhibition of molting M (%)	Efficacy E (%)
4D8	Endopeptidase	40*/54**	7*/8**	44*/58**
4F8	Nucleotidase	50*/64**	17*/-9**	58*/61**
1C10	HSP70	17*	ND	ND
4D6	Glu-Ala-rich	61*	11	66*
4E6	Glu-Ala-rich	20*/46**	16**	55**
3E1	ß-adaptin (appendage region)	27*	5*	31*
2C12	Beta-amyloid precursor protein (APP)	-8***	ND	ND
4F11	Block of proliferation Bop1	-39***	ND	ND
3E10	Mannose binding lectin	-48*/-10***	ND	ND
4G11	Chloride channel	38***	30	57
3C12	RNA polymerase III	-104***	ND	ND
1A9, 1B2, 4A4	ATPase	-57***	ND	ND

Mice were immunized with cDNA-containing expression plasmid DNA as described above (*) or with 100 µg/dose of recombinant protein expressed in *E. coli* (**). I, M and E were calculated as described above. ND, not determined.

***Resulted in a pro-feeding activity. This effect could be due to the expression of cDNAs encoding for tick immunosuppressants, anticoagulants and other proteins with low antigenicity and a pro-feeding activity. Alternatively, they could encode for proteins homologous to host proteins with anti-tick activity, which neutralization results in a tick pro-feeding activity.

In view of the above, it will be seen that the several objectives of the invention are achieved and other advantageous results attained. As various changes could be made in the above DNA molecules, proteins, etc. without departing from the scope of the invention, it is intended that all matter contained in the above description or shown in the accompanying drawings shall be interpreted as illustrative and not in a limiting sense. While the invention has been described with a certain degree of particularity, it is understood that the invention is not limited to the embodiment(s) set for herein for purposes of exemplification, but is to be limited only by the scope of the attached claim or claims, including the full range of equivalency to which each element thereof is entitled.

WHAT IS CLAIMED IS:

1. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 1-117 of SEQ ID NO: 1.

2. An expression vector comprising the isolated cDNA molecule of claim 1.

3. An isolated cell transformed by the expression vector of claim 2.

4. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 1, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 1, and (iii) a combination of the isolated cDNA molecule of claim 1 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

5. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 4.

6. The polypeptide encoded by the isolated cDNA molecule of claim 1.

7. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 80-575 of SEQ ID NO: 3.

8. An expression vector comprising the isolated cDNA molecule of claim 7.

9. An isolated cell transformed by the expression vector of claim 8.

10. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of

claim 7, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 7, and (iii) a combination of the isolated cDNA molecule of claim 7 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

11. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 10.

12. The polypeptide encoded by the isolated cDNA molecule of claim 7.

13. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 10-951 of SEQ ID NO: 5.

14. An expression vector comprising the isolated cDNA molecule of claim 13.

15. An isolated cell transformed by the expression vector of claim 14.

16. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 13, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 13, and (iii) a combination of the isolated cDNA molecule of claim 13 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

17. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 16.

18. The polypeptide encoded by the isolated cDNA molecule of claim 13.

19. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 1-697 of SEQ ID NO: 7.

20. An expression vector comprising the isolated cDNA molecule of claim 19.

21. An isolated cell transformed by the expression vector of claim 20.

22. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 19, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 19, and (iii) a combination of the isolated cDNA molecule of claim 19 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

23. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 22.

24. The polypeptide encoded by the isolated cDNA molecule of claim 19.

25. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 198-1025 of SEQ ID NO: 9.

26. An expression vector comprising the isolated cDNA molecule of claim 25.

27. An isolated cell transformed by the expression vector of claim 26.

28. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 25, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 25, and (iii) a combination of the isolated cDNA molecule of claim 25 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

29. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 28.

30. The polypeptide encoded by the isolated cDNA molecule of claim 25.

31. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 3-578 of SEQ ID NO: 11.

32. An expression vector comprising the isolated cDNA molecule of claim 31.

33. An isolated cell transformed by the expression vector of claim 32.

34. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 31, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 31, and (iii) a combination of the isolated cDNA molecule of claim 31 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

35. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 34.

36. The polypeptide encoded by the isolated cDNA molecule of claim 31.

37. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 1-1119 of SEQ ID NO: 13.

38. An expression vector comprising the isolated cDNA molecule of claim 37.

39. An isolated cell transformed by the expression vector of claim 38.

40. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 37, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 37, and (iii) a combination of the isolated cDNA molecule of claim 37 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

41. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 40.

42. The polypeptide encoded by the isolated cDNA molecule of claim 37.

43. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 51-1544 of SEQ ID NO: 15.

44. An expression vector comprising the isolated cDNA molecule of claim 43.

45. An isolated cell transformed by the expression vector of claim 44.

46. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 43, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 43, and (iii) a combination of the isolated cDNA molecule of claim 43 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

47. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 46.

48. The polypeptide encoded by the isolated cDNA molecule of claim 43.

49. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 31-2295 of SEQ ID NO: 17.

50. An expression vector comprising the isolated cDNA molecule of claim 49.

51. An isolated cell transformed by the expression vector of claim 50.

52. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 49, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 49, and (iii) a combination of the isolated cDNA molecule of claim 49 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

53. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 52.

54. The polypeptide encoded by the isolated cDNA molecule of claim 49.

55. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 6-332 of SEQ ID NO: 19.

56. An expression vector comprising the isolated cDNA molecule of claim 55.

57. An isolated cell transformed by the expression vector of claim 56.

58. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 55, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 55,

and (iii) a combination of the isolated cDNA molecule of claim 55 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

59. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 58.

60. The polypeptide encoded by the isolated cDNA molecule of claim 55.

61. An isolated cDNA molecule which encodes an *Ixodes* associated antigenic polypeptide, said molecule having a nucleotide sequence comprising at least residues 3-137 of SEQ ID NO: 21.

62. An expression vector comprising the isolated cDNA molecule of claim 61.

63. An isolated cell transformed by the expression vector of claim 62.

64. A vaccine comprising an effective immunizing amount of an immunogen selected from the group consisting of (i) the isolated cDNA molecule of claim 61, (ii) the polypeptide encoded by the isolated cDNA molecule of claim 61, and (iii) a combination of the isolated cDNA molecule of claim 61 and the encoded polypeptide, and further comprising a pharmaceutically acceptable carrier or diluent.

65. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 64.

66. The polypeptide encoded by the isolated cDNA molecule of claim 61.

67. An isolated cDNA molecule comprising a nucleotide sequence of that show in SEQ ID NO: 23.

68. An expression vector comprising the isolated cDNA molecule of claim 67.

69. An isolated cell transformed by the expression vector of claim 68.

70. A vaccine comprising an effective immunizing amount of the isolated cDNA molecule of claim 67 and a pharmaceutically acceptable carrier or diluent.

71. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 70.

72. An isolated cDNA molecule comprising a nucleotide sequence of that shown in SEQ ID NO: 24.

73. An expression vector comprising the isolated cDNA molecule of claim 72.

74. An isolated cell transformed by the expression vector of claim 73.

75. A vaccine comprising an effective immunizing amount of the isolated cDNA molecule of claim 72 and a pharmaceutically acceptable carrier or diluent.

76. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 75.

77. An isolated cDNA molecule comprising a nucleotide sequence of that shown in SEQ ID NO: 25.

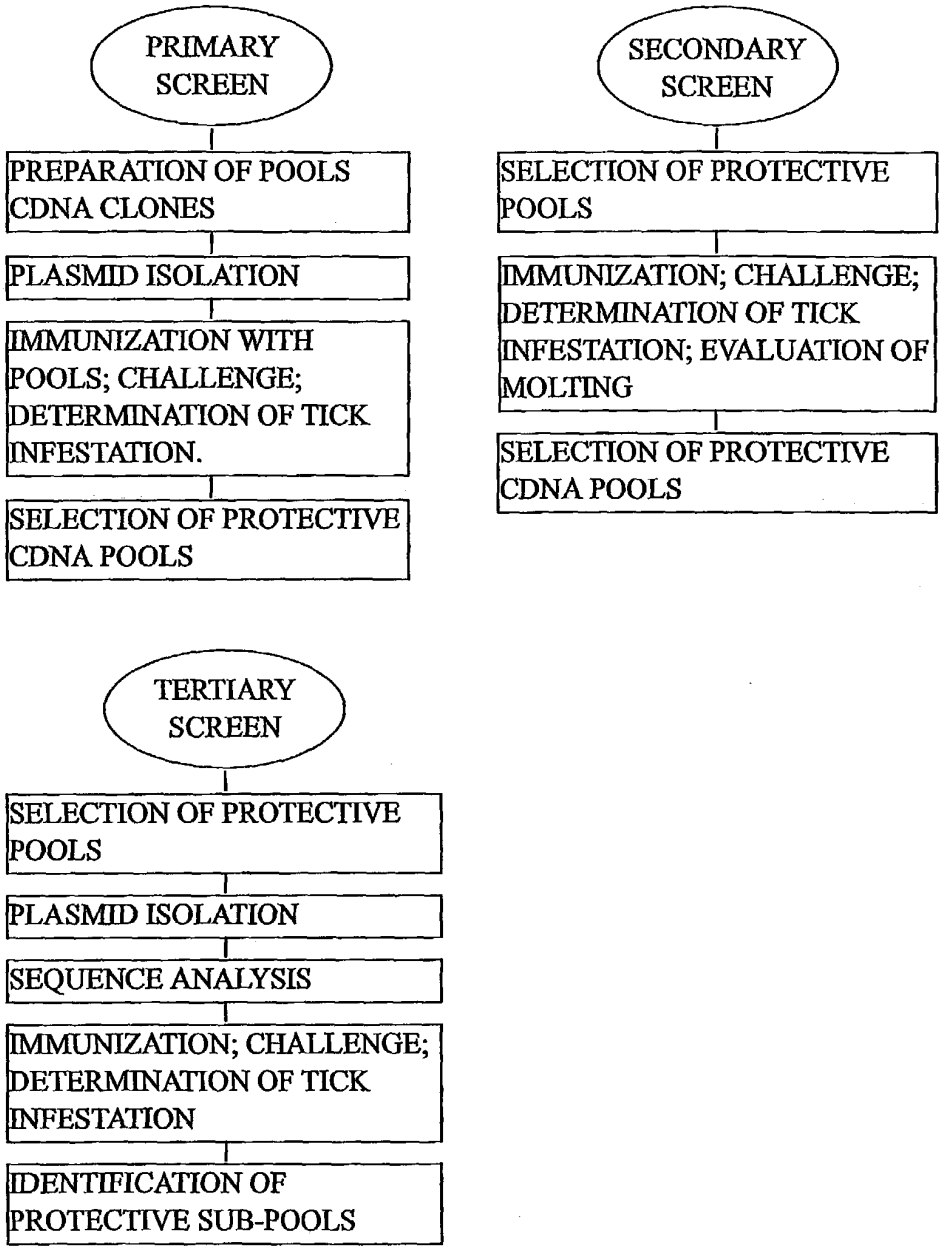
78. An expression vector comprising the isolated cDNA molecule of claim 77.

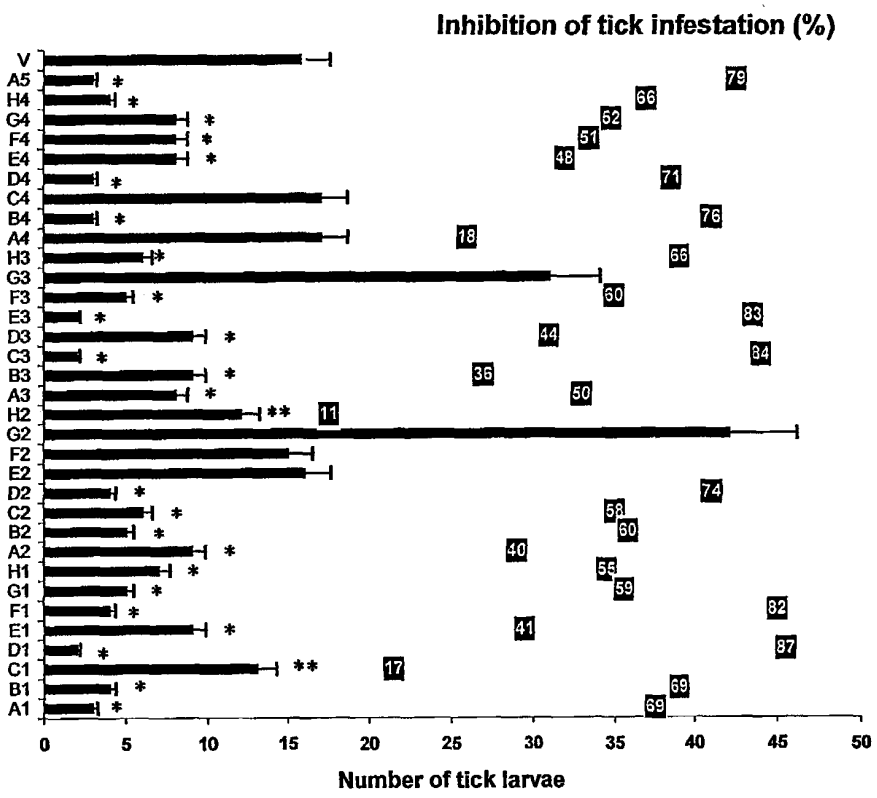
79. An isolated cell transformed by the expression vector of claim 78.

80. A vaccine comprising an effective immunizing amount of the isolated cDNA molecule of claim 77 and a pharmaceutically acceptable carrier or diluent.

81. A method of inducing an immune response in a mammal against *Ixodes* species ticks and their associated pathogens, comprising administering to the mammal the vaccine of claim 80.

FIG. 1


PRIMARY SCREEN
PREPARATION OF POOLS CDNA CLONES
PLASMID ISOLATION
IMMUNIZATION WITH POOLS; CHALLENGE; DETERMINATION OF TICK INFESTATION.
SELECTION OF PROTECTIVE CDNA POOLS
SECONDARY SCREEN
SELECTION OF PROTECTIVE POOLS
IMMUNIZATION; CHALLENGE; DETERMINATION OF TICK INFESTATION; EVALUATION OF MOLTING
SELECTION OF PROTECTIVE CDNA POOLS
TERTIARY SCREEN
SELECTION OF PROTECTIVE POOLS
PLASMID ISOLATION
SEQUENCE ANALYSIS
IMMUNIZATION; CHALLENGE; DETERMINATION OF TICK INFESTATION
IDENTIFICATION OF PROTECTIVE SUB-POOLS


Inhibition of tick infestation (%)
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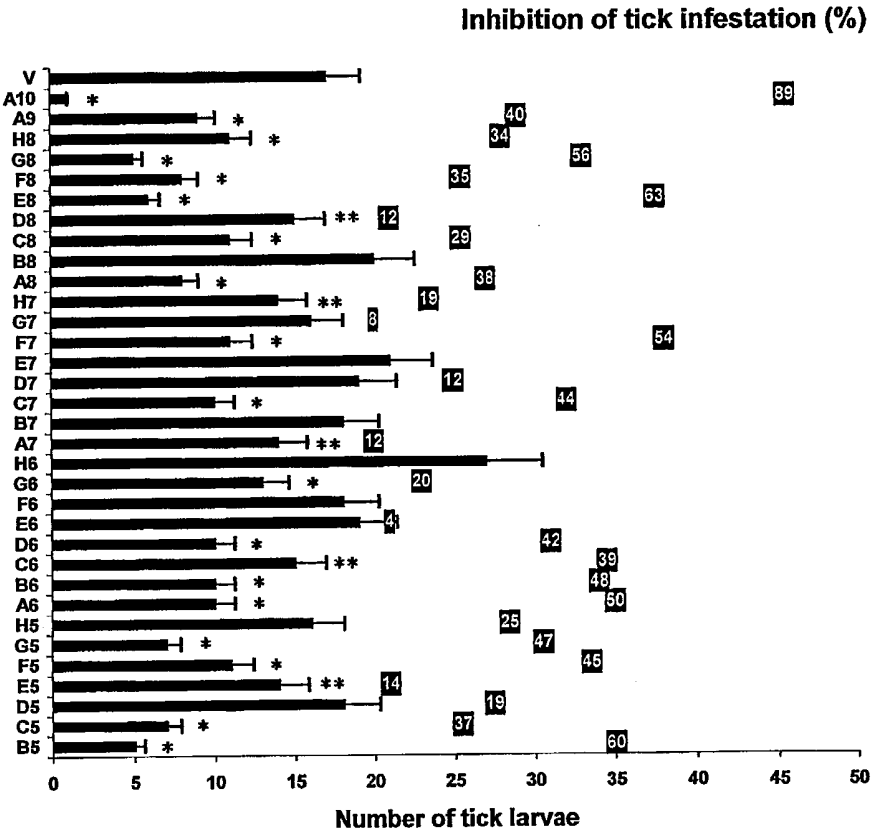
Number of tick larvae

FIG. 2A


Inhibition of tick infestation (%)
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45
14
19
37
60
0
5
10
15
20
25
30
35
40
45
50
Number of tick larvae

FIG. 2B

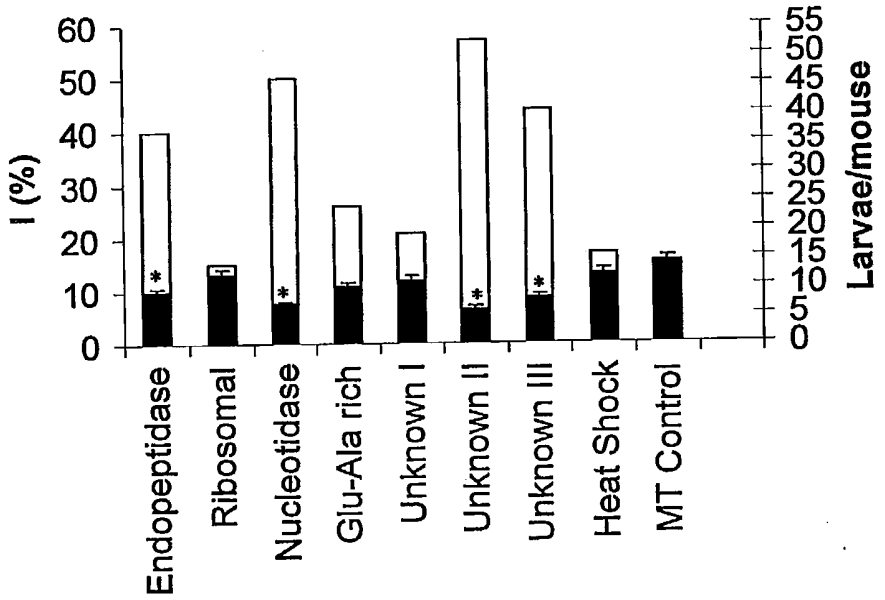
I (%)
60
50
40
30
20
10
0
55
50
45
40
35
30
25
20
15
10
5
0
Larvae/mouse
Endopeptidase
Ribosomal
Nucleotidase
Glu-Ala rich
Unknown I
Unknown II
Unknown III
Heat Shock
MT Control

FIG. 3

Fuente2.ST25.txt
SEQUENCE LISTING

<110> De La Fuente, Jose de Jesus
Kocan, Katherine M.
Garcia-Almazan, Consuelo
Garcia-Garcia, Jose Carlos
Blouin, Edwin F.

<120> Protective Antigens for the Control of Ixodes Species Infestations

<130> 03-368

<150> 60/376,251
<151> 2002-04-29

<160> 25

<170> PatentIn version 3.2

<210> 1
<211> 349
<212> DNA
<213> Ixodes scapularis

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gttaatgatg tgttgtgcaa ttcgaatgtg gctgcaacct cgctagagaa catagtcgac 180

cagctgtagt gctctagtat taaccaagaa gcagtattct gccgtcatat gtacaggcag 240

atttgttacg gcattttcag ctttttttta tacaaaatgt agttcttgtt taaaaaaaac 300

ctaaaataaa acaaagccac aaaaaaaaaa aaaaaaaaaa aaaaaaaaa 349

<210> 2
<211> 38
<212> PRT
<213> Ixodes scapularis

<400> 2

Met Glu Ile Ser Val Lys Pro Arg Pro Thr Lys Arg Lys Arg Lys Ala
1 5 10 15

Ile Ile Ile Met Ala Arg Met Arg Thr Ala Phe Pro Thr Arg Ser Gly
20 25 30

Asn Ser Phe Ser Arg Thr
35

<210> 3
<211> 2693
<212> DNA
<213> Ixodes scapularis

<220>
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<222> (685)..(685)
<223> n is a, c, g, or t

<220>
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<222> (1962)..(1962)
<223> n is a, c, g, or t

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gctgcatagt ccaaacggaa gatcgcccaa acgacggaga tgtatgcctt tgtcggtcac 180

acaagcagcg actcccccaa caagggcaca ccaaatcaac ccttcaccct tcggtgaagt 240

gccaccgaaa ttaacttcag aggagatagc ggccaacatt cgggaggaaa tgcgacgtct 300

gcagcggcgc aagcagctct gcttctcgtc tcccctggag tcgggctccc cgtcggcgac 360

tccccctgcg gccgattgcg gaccagcctc ccccacgggc ctgtcccccg ggggcctgct 420

gtcgcccgtg cgcagggacc aacccctctt caccttccgc caggtggggc tcatctgcga 480

gcgcatgatg aaggagcgcg agagccagat acgcgacgag tacgaccacg ttctgtctgc 540

caagctggca gagcagtacg acacatttgt caagtttacg tacgaccaaa ttcagaagcg 600

gtttgagggt gccactccaa gctatttgtc ataacatgat gggcatctgc aaacaagcaa 660

ggaactttga gggtttgtgc taganggaag aaacccatgg tggggaagga cacaagacca 720

acacttagac tcggcaagca agccagatcc tgtggggtgc ggggacgggg ggaatgagtc 780

cagtggtgtc ttcggagttt tttttttcc ttctcccttt ccctcgtctt ctttttggca 840

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tgagtatggt tagtcaccgt ttacttttca ggaggggat gactgaggaa cggagccgcc 1140

ccaactctcg tttgtctttt atttttagga tactttctct gtggcgagaa tttgtgtgtg 1200

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tggctatatt acttgcattg agggggagga ggaatgctgg acctcgagca gagccagcaa 1380

gtattttgga aaggaataaa aacaaaaatt ggcttagtgt acagatgtat aatatatatg 1440

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aataaaggca ctctctcagt acctaaaaaa aaaaaaaaaa aaaaaaaaaa aaa 2693

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<211> 184
<212> PRT
<213> Ixodes scapularis

<400> 4

Met Ala Cys Ala Thr Leu Lys Arg Thr His Asp Trp Asp Pro Leu His
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Ser Pro Asn Gly Arg Ser Pro Lys Arg Arg Arg Cys Met Pro Leu Ser
20 25 30

Val Thr Gln Ala Ala Thr Pro Pro Thr Arg Ala His Gln Ile Asn Pro
35 40 45

Ser Pro Phe Gly Glu Val Pro Pro Lys Leu Thr Ser Glu Glu Ile Ala
50 55 60

Ala Asn Ile Arg Glu Glu Met Arg Arg Leu Gln Arg Arg Lys Gln Leu
65 70 75 80

Cys Phe Ser Ser Pro Leu Glu Ser Gly Ser Pro Ser Ala Thr Pro Pro
85 90 95

Ala Ala Asp Cys Gly Pro Ala Ser Pro Thr Gly Leu Ser Pro Gly Gly
100 105 110

Leu Leu Ser Pro Val Arg Arg Asp Gln Pro Leu Phe Thr Phe Arg Gln
115 120 125

Val Gly Leu Ile Cys Glu Arg Met Met Lys Glu Arg Glu Ser Gln Ile
130 135 140

Arg Asp Glu Tyr Asp His Val Leu Ser Ala Lys Leu Ala Glu Gln Tyr
145 150 155 160

Asp Thr Phe Val Lys Phe Thr Tyr Asp Gln Ile Gln Lys Arg Phe Glu
165 170 175

Gly Ala Thr Pro Ser Tyr Leu Ser
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<210> 5
<211> 1821
<212> DNA
<213> Ixodes scapularis

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<223> n is a, c, g, or t

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<223> n is a, c, g, or t

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<222> (1606)..(1606)
<223> n is a, c, g, or t

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<221> misc_feature
<222> (1623)..(1623)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (1762)..(1762)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (1789)..(1789)
<223> n is a, c, g, or t

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ggaatcgtcg aaaaggaagg catcaatgac ctgcaaacgg aggcagacag atctgttcag 180

cgctgcattg tgacttcgct ctcgagacag ttcccaaaac tgacaataat tggtgaagag 240

actctggagg agaaaaagat cagcgacgac tggatcatca ccgagcatga caaggatgtc 300

ctggccactt ctctgccgga caacctgaag aacatcaaag aggaagattt ggtagtctgg 360

gttgatcctc tggatggaac caaggagtac acacagggtt tcctggacca cgtgacgatc 420

ctggtgggga ttgcggttga cggtaaggca gtgggtggag tgatccacca gccgtactac 480

aactaccagg tggagaagga cgtctacaag cagggacgta ccatgtgggg cattgtcggc 540

gtcggtgcct ttgggatctc gcgcattgcg cctccggaga acaagaggat catcactacg 600

acgcgctccc attccagccc caccatcaac agctgcattg aagccatgaa tccggacgag 660

gtgctgcgag ttggaggtgc cgggcacaag gtgctgctgt tgattgaggg caaggctcac 720

gcttacgtgt ttcccagcaa agggtgcaag aaatgggaca cttgtgcccc cgaagcgatt 780

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cgttgtccgt tgcgatcaca ctcaagtcgc gtttttcctt taactttgtg gtgatgcggt 1020

tcaaagtctt atactattag tgttttggtg gtccaaatat tattactaaa aaaacccgga 1080

gacatgggac acaaaaaaat ggaggggcgg gacaataagg tctcgaacac agctcgtaca 1140

gaatttttta aaataatgtt gatttcaggt ttatttgtgg aaactctgaa attaaccgtt 1200

atgtcattat ttgggttgtg ccgtttgaaa ttttatgaaa tacgtaatag ctgcacgcat 1260

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cacttacatt gcttgatcgt tgaattaatt ttttagctga tgttaaggac acttataata 1560

attaaggaaa tgagatcgat cttgagcttg tttgngcctc tgtaanaatt gatgctcttt 1620

canacctaat gcttaatgca acaataatta tcaagtaatc cttactcagg tgtcagatat 1680

gcaagcagat gccaatgctt ctgttcattg agtggcaaaa ggcattgctc tttgtcacat 1740

tgcatgcatt tatgacagcc cnccttaata aactataatg cagctaatnt gaaaaaaaaa 1800

aaaaaaaaaa aaaaaaaaaa a 1821

<210> 6
<211> 316
<212> PRT
<213> Ixodes scapularis

<400> 6

Met Ala Ser Cys Gly Ala Ser Ala Thr Gly Pro Leu Val Leu Arg Val
1 5 10 15

Ile Ser Asn Thr Val Lys Ile Val Asn Ser Ala Gly Lys Ile Ile Lys
20 25 30

Asp Ile Met Asn Ser Gly Asn Leu Gly Ile Val Glu Lys Glu Gly Ile
35 40 45

Asn Asp Leu Gln Thr Glu Ala Asp Arg Ser Val Gln Arg Cys Ile Val
50 55 60

Thr Ser Leu Ser Arg Gln Phe Pro Lys Leu Thr Ile Ile Gly Glu Glu
65 70 75 80

Thr Leu Glu Glu Lys Lys Ile Ser Asp Asp Trp Ile Ile Thr Glu His
85 90 95

Asp Lys Asp Val Leu Ala Thr Ser Leu Pro Asp Asn Leu Lys Asn Ile
100 105 110

Lys Glu Glu Asp Leu Val Val Trp Val Asp Pro Leu Asp Gly Thr Lys
115 120 125

Glu Tyr Thr Gln Gly Phe Leu Asp His Val Thr Ile Leu Val Gly Ile
130 135 140

Ala Val Asp Gly Lys Ala Val Gly Gly Val Ile His Gln Pro Tyr Tyr
145 150 155 160

Asn Tyr Gln Val Glu Lys Asp Val Tyr Lys Gln Gly Arg Thr Met Trp
165 170 175

Gly Ile Val Gly Val Gly Ala Phe Gly Ile Ser Arg Ile Ala Pro Pro
180 185 190

Glu Asn Lys Arg Ile Ile Thr Thr Thr Arg Ser His Ser Ser Pro Thr
195 200 205

Ile Asn Ser Cys Ile Glu Ala Met Asn Pro Asp Glu Val Leu Arg Val
210 215 220

Gly Gly Ala Gly His Lys Val Leu Leu Leu Ile Glu Gly Lys Ala His
225 230 235 240

Ala Tyr Val Phe Pro Ser Lys Gly Cys Lys Lys Trp Asp Thr Cys Ala
245 250 255

Pro Glu Ala Ile Leu His Ala Thr Gly Gly Leu Leu Thr Asp Val His
260 265 270

Gly Asn Arg Leu Glu Tyr His Lys Asp Val Glu His Val Asn Ala Gly
275 280 285

Gly Val Leu Ala Thr Cys Leu Lys Glu Gln His Glu Trp Phe Lys Asn
290 295 300

His Ile Pro Glu Asp Val Arg Lys Thr Leu Pro Leu
305 310 315

Fuente2.ST25.txt

<210> 7
<211> 697
<212> DNA
<213> Ixodes scapularis

<220>
<221> misc_feature
<222> (573)..(573)
<223> n is a, c, g, or t

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gcctccaacg ataccttctt taagggggac gactgcaagc agtggtatcg gtggcccgag 120

atgttcgaca gcggcatgga caaggacggg gcaggctttt acctgctctc ctacctgctg 180

tacgtcatgt ggagtgtgct cttcgccacc ctggccgtca tgctcgttcg caccttcgcg 240

ccctatgcct gtggatctgg aatcccggag atcaagacga ttctgagcgg cttcatcatc 300

cgcggctacc tgggcaagtg gacgctgacc atcaaatcag tgtgtctggt gctggccgtc 360

ggggcgggcc tcagcctggg caaagagggg cccctggtgc acgtggcctg ctgcatcggg 420

aacatcttct cctacctctt ccccaagtac ggcaagaatg aggccaagaa gagggagatc 480

ctgtcggctg ccgccgccgc gggagtttct gtggcctttg gggctcccat cggcggtgtt 540

ctcttcagcc tcgaagaggt gagctactac ttncccttga agacgctgtg gcgttccttc 600

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ctggtgatgt tctacgtcga gtacgacttt ccctggc 697

<210> 8
<211> 232
<212> PRT
<213> Ixodes scapularis

<220>
<221> misc_feature
<222> (191)..(191)
<223> Xaa can be any naturally occurring amino acid

<400> 8

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1 5 10 15

Gln Cys Cys Trp Ala Ser Asn Asp Thr Phe Phe Lys Gly Asp Asp Cys
20 25 30

Lys Gln Trp Tyr Arg Trp Pro Glu Met Phe Asp Ser Gly Met Asp Lys
35 40 45

Asp Gly Ala Gly Phe Tyr Leu Leu Ser Tyr Leu Leu Tyr Val Met Trp
50 55 60

Ser Val Leu Phe Ala Thr Leu Ala Val Met Leu Val Arg Thr Phe Ala
65 70 75 80

Pro Tyr Ala Cys Gly Ser Gly Ile Pro Glu Ile Lys Thr Ile Leu Ser
85 90 95

Gly Phe Ile Ile Arg Gly Tyr Leu Gly Lys Trp Thr Leu Thr Ile Lys
100 105 110

Ser Val Cys Leu Val Leu Ala Val Gly Ala Gly Leu Ser Leu Gly Lys
115 120 125

Glu Gly Pro Leu Val His Val Ala Cys Cys Ile Gly Asn Ile Phe Ser
130 135 140

Tyr Leu Phe Pro Lys Tyr Gly Lys Asn Glu Ala Lys Lys Arg Glu Ile
145 150 155 160

Leu Ser Ala Ala Ala Ala Ala Gly Val Ser Val Ala Phe Gly Ala Pro
165 170 175

Ile Gly Gly Val Leu Phe Ser Leu Glu Glu Val Ser Tyr Tyr Xaa Pro
180 185 190

Leu Lys Thr Leu Trp Arg Ser Phe Phe Cys Ala Leu Val Ala Ala Ser
195 200 205

Val Leu Arg Ser Ile Asn Pro Phe Gly Asn Asp His Leu Val Met Phe
210 215 220

Tyr Val Glu Tyr Asp Phe Pro Trp
225 230

<210> 9
<211> 1221
<212> DNA
<213> Ixodes scapularis

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ctaacgtctc ggatctgctg ttcaaagtcc cgggcgatca agccgtattt gttgtccagc 180

tgccaagtgc gtcgaatatg atgccgaaaa agaaagaatc agtcgcgagc tctaaagaag 240

acgcgccgat cgacgtgatc ggcctgccct cccacaaacg acacaagaag cacaagcaca 300

aaaagcacaa gcgcaagcga ggcacggacc aagacgaaga ccaatcgccc gccgcgagcc 360

cgcagagcgg tggcgagggt agcagcagca agcccgcgct caagctcaag atcaagatcg 420

gcggacagac ggtcgagaag aacgtgacca agctgaaaca gcagcggccg ccgccgccgg 480

accctagcga agccgatctc gccgaactcc tgatgaaacc caactcgggc gatacgagcg 540

cagacagcga tgacgaagag gaagcctggc tcgaagccct cgagtccggc aggctcgaag 600

aggtcgacga cgagctccgc aaaatgaagg acccgaccct gatgacggcc aggcagcggg 660

ccctgctcga gagcaagtcg cagaaggacg aggtcccggc gacggggatg gcnggcgtcc 720

gcggagcccg tcaaagagat gtccgaggag atgattcagc ggcggatgct gcgggccaaa 780

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agcctcgagt gctacaagac gaacatgctg cagatgtgcg tctgagcggg cagctaggct 1140

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aaaaaaaaaa aaaaaaaaaa a 1221

<210> 10
<211> 275
<212> PRT
<213> Ixodes scapularis

<400> 10

Met Met Pro Lys Lys Lys Glu Ser Val Ala Ser Ser Lys Glu Asp Ala
1 5 10 15

Pro Ile Asp Val Ile Gly Leu Pro Ser His Lys Arg His Lys Lys His
20 25 30

Lys His Lys Lys His Lys Arg Lys Arg Gly Thr Asp Gln Asp Glu Asp
35 40 45

Gln Ser Pro Ala Ala Ser Pro Gln Ser Gly Gly Glu Gly Ser Ser Ser
50 55 60

Lys Pro Ala Leu Lys Leu Lys Ile Lys Ile Gly Gly Gln Thr Val Glu
65 70 75 80

Lys Asn Val Thr Lys Leu Lys Gln Gln Arg Pro Pro Pro Pro Asp Pro
85 90 95

Ser Glu Ala Asp Leu Ala Glu Leu Leu Met Lys Pro Asn Ser Gly Asp
100 105 110

Thr Ser Ala Asp Ser Asp Asp Glu Glu Glu Ala Trp Leu Glu Ala Leu
115 120 125

Glu Ser Gly Arg Leu Glu Glu Val Asp Asp Glu Leu Arg Lys Met Lys
130 135 140

Asp Pro Thr Leu Met Thr Ala Arg Gln Arg Ala Leu Leu Glu Ser Lys
145 150 155 160

Ser Gln Lys Asp Glu Val Pro Ala Thr Gly Met Ala Gly Val Arg Gly
165 170 175

Ala Arg Gln Arg Asp Val Arg Gly Asp Asp Ser Ala Ala Asp Ala Ala
180 185 190

Gly Gln Lys Ala Glu Ala Ala Gly Arg Arg Glu Glu Arg Glu Gly Glu
195 200 205

Glu Ala Asp Asp Arg Ala Ser Ala Gln Glu Val Arg Leu Glu Ala Glu
210 215 220

Gly Gln Gln Glu Val Gly Gln Glu Glu Arg Tyr Ser Gln Gly Val Ala
225 230 235 240

Gly Gln His Ala Gly Arg His Ala Ala Leu Val Ser Arg Arg Arg Cys
245 250 255

Val Pro Ala Val Gly Ser Arg Gly Pro Gly Val Pro Arg Glu Asp Asp
260 265 270

Val Arg His
275

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<211> 1942
<212> DNA
<213> Ixodes scapularis

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tgcagctggg aaccaacggt cccgtgcaga agatggaccc cctcaccaac cttcaggtgg 180

ccatcaagaa caatgtggac gtgttctact tcagctgcct ggtgcccatg cacgtgctga 240

gcacggagga cggcctgatg gacaagcggg tgttcctggc cacctggaaa gacatccccg 300

cccaaaacga ggtccagtac accctcgaca acgtcaacct cactgcagac caagtttccc 360

agaagctgca gaacaacaac attttcacga tagccaagag gaacgtggac ggccaggaca 420

tgctgtacca gtccctgaag ctcaccaacg gcatttgggt gttggcggag ctcaagatac 480

agcccggcaa tccaaggatc acgttgtctt tgaagacaag agcacctgaa gtggcagcag 540

gtgtacaaca aacttacgaa ctcattctac acagctgagg ctgctgtgaa tgaaactctt 600

ctcccacccc cttcttttga tggcagtcaa tgtctcgttt cattttcttg ttttcttttg 660

cggcgtgcta cggaacaagg tcctacattc ccaagttata tggtgttgtc gcgtaggggg 720

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aaaaagaaaa agtgaaaacg gaaaaatgaa aaattttcca gttgcttcaa attaacattc 840

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tgaaaatggt tgctttttat tggtatcccc tatcacaccg agcacgaaca taagaaatcc 960

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tgaaactctg ctccgccgct gctagtgtca tcacgggacg accatcgcgt tttctctgac 1320

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agccctgccc tttcggtgtg tgtacaagca tctctgtgta acatgaacta ctttacatga 1440

actacattgc atgaacggga gaagtttagt tgtttttttg ttttttttt caggtgacta 1500

tgtcaacaga ttagaaccat tttttggaac ggctggaaag ataaccgctc attttgtttc 1560

tactaaaaga ctacgaaaag tgttgacttt ttgcatcggt ttggcaacgt ttgtttggca 1620

tgcatgtagt tgagcgtaat ggtatcaccc ctcgtaaaca ataacagtgc aatggagcag 1680

tactgtagtg tccattaaag agcgagagtt tggttaaagg ttgttaattg aggtccgtgt 1740

tatcctttga gtaggagagc ggcacttttt gcaaatagcg ctgctggggg cgtcatatct 1800

gccctccaaa acatgcacat tttaagtgtg aattgttgcg gcggcttgta caagtatgtg 1860

tgttatgtgt agaaaaagaa ctcttaatta aaatatttgt ggccaaaacg tcaaaaaaaa 1920

aaaaaaaaaa aaaaaaaaaa aa 1942

<210> 12
<211> 191
<212> PRT
<213> Ixodes scapularis

<400> 12

Met Gln Ala Met Thr Gly Phe Ala Val Gln Phe Asn Lys Asn Ser Phe
1 5 10 15

Gly Leu Thr Pro Ala Gln Pro Leu Gln Leu Gln Ile Pro Leu Gln Pro
20 25 30

Asn Phe Pro Ala Asp Ala Ser Leu Gln Leu Gly Thr Asn Gly Pro Val
35 40 45

Gln Lys Met Asp Pro Leu Thr Asn Leu Gln Val Ala Ile Lys Asn Asn
50 55 60

Val Asp Val Phe Tyr Phe Ser Cys Leu Val Pro Met His Val Leu Ser
65 70 75 80

Thr Glu Asp Gly Leu Met Asp Lys Arg Val Phe Leu Ala Thr Trp Lys
85 90 95

Asp Ile Pro Ala Gln Asn Glu Val Gln Tyr Thr Leu Asp Asn Val Asn
100 105 110

Leu Thr Ala Asp Gln Val Ser Gln Lys Leu Gln Asn Asn Asn Ile Phe
115 120 125

Thr Ile Ala Lys Arg Asn Val Asp Gly Gln Asp Met Leu Tyr Gln Ser
130 135 140

Leu Lys Leu Thr Asn Gly Ile Trp Val Leu Ala Glu Leu Lys Ile Gln
145 150 155 160

Pro Gly Asn Pro Arg Ile Thr Leu Ser Leu Lys Thr Arg Ala Pro Glu
165 170 175

Val Ala Ala Gly Val Gln Gln Thr Tyr Glu Leu Ile Leu His Ser
180 185 190

<210> 13
<211> 1428
<212> DNA
<213> Ixodes scapularis

<220>
<221> misc_feature
<222> (701)..(701)
<223> n is a, c, g, or t

<400> 13
cgcgccgtgc agaagctgcg tcgggaggtt gagaaggcaa agaggaccct gtccactgct 60

caccaggcca ggatcgagat tgaatcgttc ttcgagggag aggacttcag tgagaccctg 120

actcgtgcta agtttgagga gctgaacatg gacctttttcc gttccaccat gaagcctgtt 180

cagaaggtac tcgaggatgg tgacctcaag aagactgatg tggacgagat tgtgcttgtc 240

ggaggttcca ccaggatccc caaggttcaa cagctggtca aggagttctt caatggcaag 300

gaacccaccc gtggcatcaa ccccgacgaa gcagtcgcct acggtgccgc cgtgcaggct 360

ggagtcctcg gcggagagga agacactggg gacctcgtgc tgttggacgt gaaccctctg 420

accctcggca tcgagacagt gggaggcgtc atgacgaaac tgatcccccg taacacagtc 480

atccccacga agaagtctca gatcttctcc acggcctcgg acgagcagag cactgtcacc 540

atccaggtct ttgaggggga gcgtcccctg acaaaggaca accaccagct gggcaagttc 600

gacctgactg gcatcccacc tgctcctcga ggtgtgcccc aaatcgaggt gaccttcgag 660

attgacgtca acggtatcct gcgggtcagt gcagaggaca ngggtacagg caacaagcag 720

aagatcacca tcaacaatga ccagaacagg ctgacgcctg aggacatcga gaggatggta 780

aaggacgccg aaaagtttgc cgacgaggac aagaaggtca aggagaaggt ggaggcccgc 840

aacgaactgg agtcttatgc ctactccctc aagaaccaga ttggagacaa ggagaagatg 900

ggaggcaagc tctccgacga ggacaagaag actattgagc aagctgtgga cgagaaaatc 960

aaatggctgg agcagcacag tgacgctgat gcggaagaac tcaaggaaca gaagaaacag 1020

ctggctgata ctgtgcagcc gattgtagcc aagctgtacc ctgcaggagg caccccaccg 1080

ccgacggaca aagatgactc tacaaaggac gagttgtaaa aacaaggcca gatctcttgg 1140

gtacagcgaa aggcatgggg cagcagcatt atcacaagtc atctgttacg atcatgagct 1200

catcatttca ccacctctac agtgctgctg ctgcctgcct tttggctggt tgagtgttct 1260

tggacctatt taccatgatc attctctgta caaaaacaat tctttctgtg ttttttttt 1320

tttcgttgta gtaacttaag ttatacagat gtcttctact gggtgggctt tctccatgag 1380

tgggaggggg ctgggtgtca aataaaagtg tttctattaa aaaaaaaa 1428

<210> 14
<211> 372
<212> PRT
<213> Ixodes scapularis

<220>
<221> misc_feature
<222> (234)..(234)
<223> Xaa can be any naturally occurring amino acid

<400> 14

Arg Ala Val Gln Lys Leu Arg Arg Glu Val Glu Lys Ala Lys Arg Thr
1 5 10 15

Leu Ser Thr Ala His Gln Ala Arg Ile Glu Ile Glu Ser Phe Phe Glu
20 25 30

Gly Glu Asp Phe Ser Glu Thr Leu Thr Arg Ala Lys Phe Glu Glu Leu
35 40 45

Asn Met Asp Leu Phe Arg Ser Thr Met Lys Pro Val Gln Lys Val Leu
50 55 60

Glu Asp Gly Asp Leu Lys Lys Thr Asp Val Asp Glu Ile Val Leu Val
65 70 75 80

Gly Gly Ser Thr Arg Ile Pro Lys Val Gln Gln Leu Val Lys Glu Phe
85 90 95

Phe Asn Gly Lys Glu Pro Thr Arg Gly Ile Asn Pro Asp Glu Ala Val
100 105 110

Ala Tyr Gly Ala Ala Val Gln Ala Gly Val Leu Gly Gly Glu Glu Asp
115 120 125

Thr Gly Asp Leu Val Leu Leu Asp Val Asn Pro Leu Thr Leu Gly Ile
130 135 140

Glu Thr Val Gly Gly Val Met Thr Lys Leu Ile Pro Arg Asn Thr Val
145 150 155 160

Ile Pro Thr Lys Lys Ser Gln Ile Phe Ser Thr Ala Ser Asp Glu Gln
165 170 175

Ser Thr Val Thr Ile Gln Val Phe Glu Gly Glu Arg Pro Leu Thr Lys
180 185 190

Asp Asn His Gln Leu Gly Lys Phe Asp Leu Thr Gly Ile Pro Pro Ala
195 200 205

Pro Arg Gly Val Pro Gln Ile Glu Val Thr Phe Glu Ile Asp Val Asn
210 215 220

Gly Ile Leu Arg Val Ser Ala Glu Asp Xaa Gly Thr Gly Asn Lys Gln
225 230 235 240

Lys Ile Thr Ile Asn Asn Asp Gln Asn Arg Leu Thr Pro Glu Asp Ile
245 250 255

Glu Arg Met Val Lys Asp Ala Glu Lys Phe Ala Asp Glu Asp Lys Lys
260 265 270

Val Lys Glu Lys Val Glu Ala Arg Asn Glu Leu Glu Ser Tyr Ala Tyr
275 280 285

Ser Leu Lys Asn Gln Ile Gly Asp Lys Glu Lys Met Gly Gly Lys Leu
290 295 300

Ser Asp Glu Asp Lys Lys Thr Ile Glu Gln Ala Val Asp Glu Lys Ile
305 310 315 320

Lys Trp Leu Glu Gln His Ser Asp Ala Asp Ala Glu Glu Leu Lys Glu
325 330 335

Gln Lys Lys Gln Leu Ala Asp Thr Val Gln Pro Ile Val Ala Lys Leu
340 345 350

Tyr Pro Ala Gly Gly Thr Pro Pro Pro Thr Asp Lys Asp Asp Ser Thr
355 360 365

Lys Asp Glu Leu
370

<210> 15
<211> 1847

<212> DNA
<213> Ixodes scapularis

<220>
<221> misc_feature
<222> (1814)..(1814)
<223> n is a, c, g, or t

<400> 15
cgacgtgttt gtgagtgcag cggtgaactg gacggtgtcg tggccacgcg atggcagcgg 60

cggtgatgaa ctgcctacgg actgcgcttt taggcgctct cgtcgtccaa ctctacgcca 120

cgcagatagg tcaccggaaa ttcgagtaca agtacagttt caagggaccc tacctggcgc 180

agaaggatgg atcggtgcct ttctgggagt acggcggcaa ttgcatcgcc agtgaggaga 240

tggttcggat cacgccctcc ctgaagagca agaaaggatc catctggtcc aagctgccga 300

catcgttccc ttggtgggag gtggagctgg tgttccgcac cacgggtacg ggcaggatag 360

gagctgacgg cctggccttc tggtacacag acaagaagca ggcggagggt cctgtctttg 420

gaagcagcga caagtggact ggcctggcca tcttcttcga ttccttcgac aatgataaca 480

agcacaacaa cccatacatc atgggcatgg tgaacgatgg aacaaaagcc tacgatcatg 540

agagtgacgg tgccaaccaa cagctagcgg gatgccagcg ggacttccgc aacaagcctt 600

accctgtcag ggccaagata gaatacttca acaacattct cacggtgctg ttccacaacg 660

gcaacaccaa caacgacggt gactacgaga tgtgcttccg tgcggagaac gtgttcctgc 720

cgaccaacgg ccactttggg gtgtccgccg ccacgggggg cctggcagac gaccacgacg 780

ccctcaagtt cctgacgacg agcctgcatg cggagggcac gcagccggcc ctggcccagg 840

gtatggccga ctcagagaag gagaagttct ccaaggagta tgaagtatac aaggacaagc 900

tggaaaagca gaaggaggag taccggaaga cgcacccgga ggaggccgct aagcaggcca 960

tggagcacgg ccccgagcag gcctacgaca cgcagcagca gcgcgagctg cgccagatct 1020

tcgagggcca gagccacaaa ttgtttgagg ggctcaaggc actgcaccgc aagctggacg 1080

aggtgctcgg gcgccaggag cgcaccctgt cgctggtgtc ggctggcggc gccggcgtgg 1140

ccgtgggcgg tgttccgcca ccgcagatgg gtggagtgcc gtcgctgcag aggcacgaag 1200

cagagtccct gctgagcagc cagcgggagc tgctgcagac ggtggctcag gtcaagagct 1260

ttgtggccga ggtgcatcaa cgcacggcca ccctgcaaca ccaggggcg ggaggcaccc 1320

agggcctcac ggccgagcag ctgcaagtgc tccaccaggt gcgggacagc gtggccagca 1380

tgcaccggga cgtctccaac aaccagccgc agaggactgg ctgcgcgaca tcctgtctca 1440

gcactaccca cttcttgctg tttgcaacgt tgcagttggc tgtcacgctg ggctacttgg 1500

tgtacaggag cagcaaagag gcggcggcca agaagttcta ctgagtgcag atctcgagcc 1560

ttgccttgcc ctcccctccc atggagtgga ccttaacccc acagactgcc agaaaccagt 1620

gttgccagag gagccccccc cccttcttat tgggtggggt gccacagcca tcacccattc 1680

ttcgagacaa ggccactgtt tgggggggagg ggcaagagat tcatccgggg tgcgcaacaa 1740

aacatggccg tacagaggga ggggtgctcc agaactgggt cccagccaca tcgttgcgtg 1800

ggagcgcctt tctncctcac tctaaaaaaa aaaaaaaaaa aaaaaaa 1847

<210> 16
<211> 497
<212> PRT
<213> Ixodes scapularis

<400> 16

Met Ala Ala Ala Val Met Asn Cys Leu Arg Thr Ala Leu Leu Gly Ala
1 5 10 15

Leu Val Val Gln Leu Tyr Ala Thr Gln Ile Gly His Arg Lys Phe Glu
20 25 30

Tyr Lys Tyr Ser Phe Lys Gly Pro Tyr Leu Ala Gln Lys Asp Gly Ser
35 40 45

Val Pro Phe Trp Glu Tyr Gly Gly Asn Cys Ile Ala Ser Glu Glu Met
50 55 60

Val Arg Ile Thr Pro Ser Leu Lys Ser Lys Lys Gly Ser Ile Trp Ser
65 70 75 80

Lys Leu Pro Thr Ser Phe Pro Trp Trp Glu Val Glu Leu Val Phe Arg
85 90 95

Thr Thr Gly Thr Gly Arg Ile Gly Ala Asp Gly Leu Ala Phe Trp Tyr
100 105 110

Thr Asp Lys Lys Gln Ala Glu Gly Pro Val Phe Gly Ser Ser Asp Lys
115 120 125

Trp Thr Gly Leu Ala Ile Phe Phe Asp Ser Phe Asp Asn Asp Asn Lys
130 135 140

His Asn Asn Pro Tyr Ile Met Gly Met Val Asn Asp Gly Thr Lys Ala
145 150 155 160

Tyr Asp His Glu Ser Asp Gly Ala Asn Gln Gln Leu Ala Gly Cys Gln
165 170 175

Arg Asp Phe Arg Asn Lys Pro Tyr Pro Val Arg Ala Lys Ile Glu Tyr
180 185 190

Phe Asn Asn Ile Leu Thr Val Leu Phe His Asn Gly Asn Thr Asn Asn
195 200 205

Asp Gly Asp Tyr Glu Met Cys Phe Arg Ala Glu Asn Val Phe Leu Pro
210 215 220

Thr Asn Gly His Phe Gly Val Ser Ala Ala Thr Gly Gly Leu Ala Asp
225 230 235 240

Asp His Asp Ala Leu Lys Phe Leu Thr Thr Ser Leu His Ala Glu Gly
245 250 255

Thr Gln Pro Ala Leu Ala Gln Gly Met Ala Asp Ser Glu Lys Glu Lys
260 265 270

Phe Ser Lys Glu Tyr Glu Val Tyr Lys Asp Lys Leu Glu Lys Gln Lys
275 280 285

Glu Glu Tyr Arg Lys Thr His Pro Glu Glu Ala Ala Lys Gln Ala Met
290 295 300

Glu His Gly Pro Glu Gln Ala Tyr Asp Thr Gln Gln Gln Arg Glu Leu
305 310 315 320

Arg Gln Ile Phe Glu Gly Gln Ser His Lys Leu Phe Glu Gly Leu Lys
325 330 335

Ala Leu His Arg Lys Leu Asp Glu Val Leu Gly Arg Gln Glu Arg Thr
340 345 350

Leu Ser Leu Val Ser Ala Gly Gly Ala Gly Val Ala Val Gly Gly Val
355 360 365

Pro Pro Pro Gln Met Gly Gly Val Pro Ser Leu Gln Arg His Glu Ala
370 375 380

Glu Ser Leu Leu Ser Ser Gln Arg Glu Leu Leu Gln Thr Val Ala Gln
385 390 395 400

Val Lys Ser Phe Val Ala Glu Val His Gln Arg Thr Ala Thr Leu Gln
405 410 415

His Gln Gly Ala Gly Gly Thr Gln Gly Leu Thr Ala Glu Gln Leu Gln
420 425 430

Val Leu His Gln Val Arg Asp Ser Val Ala Ser Met His Arg Asp Val
435 440 445

Ser Asn Asn Gln Pro Gln Arg Thr Gly Cys Ala Thr Ser Cys Leu Ser
450 455 460

Thr Thr His Phe Leu Leu Phe Ala Thr Leu Gln Leu Ala Val Thr Leu
465 470 475 480

Gly Tyr Leu Val Tyr Arg Ser Ser Lys Glu Ala Ala Ala Lys Lys Phe
485 490 495

Tyr

<210> 17
<211> 2475
<212> DNA
<213> Ixodes scapularis

<220>
<221> misc_feature
<222> (1342)..(1342)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (1388)..(1388)
<223> n is a, c, g, or t

<400> 17
catcactagt agcgagacac gtgcgtaaaa atggggccca aaacgctgtc taagcagccc 60

gctaaagctt cttcatccac ttccaagcgc accgccggcc ccacaataag caagcagacg 120

gaggacagcg atgacgaagg gtcaagcagc gcctactccg acttggagga ctccgaagga 180

gccgacagca gcgactcgaa cgatttgtcg gacacggagg cgtcggagga tgactacgat 240

gactcccaag acgaagaaaa cacgaagatt actttgactg gggtggaggg gaaggacctt 300

gagttgaggg ggaaggacca ggaggcaccg gtggagtctg gcaaaaggtc ggcatggcac 360

cggcagcaag aggacgccaa ggaggacaga cgaacgcaag tggtggaaga tgaatatgcc 420

tttgactctt ccgacgaaga ggacgttcgc aacacggttg gcaacattcc tctggagtgg 480

tacgagcact atccgcacat cggttatgat ctggaaggca agccaatcct gaagccgcct 540

cgggttagtg acctggacga cttcctgagg aaaatggatg accccaacta ttggaggacg 600

gtgaaggaca agagcacggg acaggacgtt gtcctgaccg acgaagatgt ggacctgatt 660

cagaggctgc agaaaggaca gttccccagc tcgacgactg acccttacga gccatttgag 720

gacatctttt cgcacgagac catgatccac ccggtgacca ggcaccctcc ccagaaacgc 780

agcttcgtgc cttcaaggat agaaaaagca atggtgtcaa agatggtgca cgcaatcaag 840

atgggctgga tcaagccccg agtaaagaag catgacccag aaagattcag cctcctgtgg 900

gacaaggatg actcgacagc gggcagcaat gagcgaatgc agcgccacat cccggcaccc 960

aagatgaagc tgccgggtca tgaggagtct tacaacccgc cggccgaata cctcttcacc 1020

gaggaagagg aggccaagtg gagagagcag gagcccgaag aacggcgcat aaacttcctg 1080

cccgccaagt acccatgtct gcgcgcagtc ccagcctacg aacgcttcat tgaggagagg 1140

tttgagcgct gtctggatct ctacttgtgc ccgaggcagc ggaagatgag ggtgaatgtg 1200

gatgcagagg acctgattcc tcagctgccc aaacccaagg acctgcagcc tttcccaagc 1260

attcagtcta ttgtctatga gggtcatacg gactgtgtcc tctgcctgtc tttggagcct 1320

gcgggacagt tctttgcatc anggtccgag gacggcaccg ttcgcatttg ggagctcttg 1380

acgggcangt gcctcaagaa gttccagttc gaggcgcccg tgaagagcgt ggcctggtgt 1440

ccagttgtcg ttcccatgaa actctgcgtg gacaagactg tttccatgct ggatgccgga 1500

gttacggaca aactgctgcc gttcaccacg ggacaccgag ttgtctgccc tccccgaaga 1560

gtcctcgggc caggcggcgg tagtggagtg ggagcagacg tcggcctcct ctccagagtt 1620

cctctcccgg ggggagcgtc tgcgggtcgt tcaccgccac ggtgtggtgc aggtgacgtg 1680

gcactcgagg ggagactact ttgccactgt cacggacgag ggacaggcca ccgtgcttgt 1740

ccatcagttg tccacgcggc ggttcgcagg ctccccttca gcaaggcgaa gggcggggtg 1800

tcccgggtgc tgttccaccc gctgcgcccc ttcctgctgg tggcgtgcca gcgcacagtg 1860

cgggtctacc acctgctcaa gcaggagctg gccaagaggc tcacatccaa ttgcaagtgg 1920

atctcgtgca tgggccgtcc acccccaggt gacaatctgc tgatcggcac gtacgagaag 1980

cggctgatgt ggttcgatct ggacctctcg accaaaccgt accagcagct gcgcatacac 2040

aatgccgcca tccgcagtgt ggcgttccat ccgcgctatc cactgtttgc gtccgccggc 2100

gacgatcgca gcgtgatcgt ttcgcacggt atggtgtaca atgatttact gcaaaaccca 2160

ctgatcgtgc cactgagacg gctgaagaac catgccatca gcaagggtat gggtgtgttg 2220

gactgcgcct tccatcccca ccagccgtgg atagtcacgg ccggagcaga cagcacgctg 2280

cggctcttca cctaagccgg gacgtcgtct ggtgtacata gtgaatcgtc aagaccgtgc 2340

caataaaagg actccacacc taaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2400

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2460

aaaaaaaaaa aaaaa 2475

<210> 18
<211> 754
<212> PRT
<213> Ixodes scapularis

<220>
<221> misc_feature
<222> (438)..(438)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> misc_feature
<222> (453)..(453)
<223> Xaa can be any naturally occurring amino acid

<400> 18

Met Gly Pro Lys Thr Leu Ser Lys Gln Pro Ala Lys Ala Ser Ser Ser
1 5 10 15

Thr Ser Lys Arg Thr Ala Gly Pro Thr Ile Ser Lys Gln Thr Glu Asp
20 25 30

Ser Asp Asp Glu Gly Ser Ser Ser Ala Tyr Ser Asp Leu Glu Asp Ser
35 40 45

Glu Gly Ala Asp Ser Ser Asp Ser Asn Asp Leu Ser Asp Thr Glu Ala
50 55 60

Ser Glu Asp Asp Tyr Asp Asp Ser Gln Asp Glu Glu Asn Thr Lys Ile
65 70 75 80

Thr Leu Thr Gly Val Glu Gly Lys Asp Leu Glu Leu Arg Gly Lys Asp
85 90 95

Gln Glu Ala Pro Val Glu Ser Gly Lys Arg Ser Ala Trp His Arg Gln
100 105 110

Gln Glu Asp Ala Lys Glu Asp Arg Arg Thr Gln Val Val Glu Asp Glu
115 120 125

Tyr Ala Phe Asp Ser Ser Asp Glu Glu Asp Val Arg Asn Thr Val Gly
130 135 140

Asn Ile Pro Leu Glu Trp Tyr Glu His Tyr Pro His Ile Gly Tyr Asp
145 150 155 160

Leu Glu Gly Lys Pro Ile Leu Lys Pro Pro Arg Val Ser Asp Leu Asp
165 170 175

Asp Phe Leu Arg Lys Met Asp Asp Pro Asn Tyr Trp Arg Thr Val Lys
180 185 190

Asp Lys Ser Thr Gly Gln Asp Val Val Leu Thr Asp Glu Asp Val Asp
195 200 205

Leu Ile Gln Arg Leu Gln Lys Gly Gln Phe Pro Ser Ser Thr Thr Asp
210 215 220

Pro Tyr Glu Pro Phe Glu Asp Ile Phe Ser His Glu Thr Met Ile His
225 230 235 240

Pro Val Thr Arg His Pro Pro Gln Lys Arg Ser Phe Val Pro Ser Arg
245 250 255

Ile Glu Lys Ala Met Val Ser Lys Met Val His Ala Ile Lys Met Gly
260 265 270

Trp Ile Lys Pro Arg Val Lys Lys His Asp Pro Glu Arg Phe Ser Leu
275 280 285

Leu Trp Asp Lys Asp Asp Ser Thr Ala Gly Ser Asn Glu Arg Met Gln
290 295 300

Arg His Ile Pro Ala Pro Lys Met Lys Leu Pro Gly His Glu Glu Ser
305 310 315 320

Tyr Asn Pro Pro Ala Glu Tyr Leu Phe Thr Glu Glu Glu Glu Ala Lys
325 330 335

Trp Arg Glu Gln Glu Pro Glu Glu Arg Arg Ile Asn Phe Leu Pro Ala
340 345 350

Lys Tyr Pro Cys Leu Arg Ala Val Pro Ala Tyr Glu Arg Phe Ile Glu
355 360 365

Glu Arg Phe Glu Arg Cys Leu Asp Leu Tyr Leu Cys Pro Arg Gln Arg
370 375 380

Lys Met Arg Val Asn Val Asp Ala Glu Asp Leu Ile Pro Gln Leu Pro
385 390 395 400

Lys Pro Lys Asp Leu Gln Pro Phe Pro Ser Ile Gln Ser Ile Val Tyr
405 410 415

Glu Gly His Thr Asp Cys Val Leu Cys Leu Ser Leu Glu Pro Ala Gly
420 425 430

Gln Phe Phe Ala Ser Xaa Ser Glu Asp Gly Thr Val Arg Ile Trp Glu
435 440 445

Leu Leu Thr Gly Xaa Cys Leu Lys Lys Phe Gln Phe Glu Ala Pro Val
450 455 460

Lys Ser Val Ala Trp Cys Pro Val Val Val Pro Met Lys Leu Cys Val
465 470 475 480

Asp Lys Thr Val Ser Met Leu Asp Ala Gly Val Thr Asp Lys Leu Leu
485 490 495

Pro Phe Thr Thr Gly His Arg Val Val Cys Pro Pro Arg Arg Val Leu
500 505 510

Gly Pro Gly Gly Gly Ser Gly Val Gly Ala Asp Val Gly Leu Leu Ser
515 520 525

Arg Val Pro Leu Pro Gly Gly Ala Ser Ala Gly Arg Ser Pro Pro Arg
530 535 540

Cys Gly Ala Gly Asp Val Ala Leu Glu Gly Arg Leu Leu Cys His Cys
545 550 555 560

His Gly Arg Gly Thr Gly His Arg Ala Cys Pro Ser Val Val His Ala
565 570 575

Ala Val Arg Arg Leu Pro Phe Ser Lys Ala Lys Gly Gly Val Ser Arg
580 585 590

Val Leu Phe His Pro Leu Arg Pro Phe Leu Leu Val Ala Cys Gln Arg
595 600 605

Thr Val Arg Val Tyr His Leu Leu Lys Gln Glu Leu Ala Lys Arg Leu
610 615 620

Thr Ser Asn Cys Lys Trp Ile Ser Cys Met Gly Arg Pro Pro Pro Gly
625 630 635 640

Asp Asn Leu Leu Ile Gly Thr Tyr Glu Lys Arg Leu Met Trp Phe Asp
645 650 655

Leu Asp Leu Ser Thr Lys Pro Tyr Gln Gln Leu Arg Ile His Asn Ala
660 665 670

Ala Ile Arg Ser Val Ala Phe His Pro Arg Tyr Pro Leu Phe Ala Ser
675 680 685

Ala Gly Asp Asp Arg Ser Val Ile Val Ser His Gly Met Val Tyr Asn
690 695 700

Asp Leu Leu Gln Asn Pro Leu Ile Val Pro Leu Arg Arg Leu Lys Asn
705 710 715 720

His Ala Ile Ser Lys Gly Met Gly Val Leu Asp Cys Ala Phe His Pro
725 730 735

His Gln Pro Trp Ile Val Thr Ala Gly Ala Asp Ser Thr Leu Arg Leu
740 745 750

Phe Thr

<210> 19
<211> 447
<212> DNA
<213> Ixodes scapularis

<400> 19
caaagatgct gctgttctgc ccgacgtgcg ccaacatcct cattgtggaa caaggcttgg 60

agtgcttccg tttcgcctgc aacacatgcc cctacgtgca caacatcaag gcgaagatgt 120

cgaatcggaa gtacccgcgg ctcaaggacg tggacgacgt gctcggcggt gcagccgcct 180

gggagaatgt tgactcgacc gaagagaagt gccccaagtg tggccatgag cgggcctatt 240

ttatgcagat ccagactagg tcggccgacg agcccatgac caccttctac aagtgctgca 300

accagctctg tggccaccag tggagggact gacagatggc ggctttgacg aactcatgcc 360

cgtgcaaaat gcgtcggggg gagagagttt tggaataaaa catgcgcctt actttcataa 420

aaaaaaaaaa aaaaaaaaaa aaaaaaa 447

<210> 20

<211> 108
<212> PRT
<213> Ixodes scapularis

<400> 20

Met Leu Leu Phe Cys Pro Thr Cys Ala Asn Ile Leu Ile Val Glu Gln
1 5 10 15

Gly Leu Glu Cys Phe Arg Phe Ala Cys Asn Thr Cys Pro Tyr Val His
20 25 30

Asn Ile Lys Ala Lys Met Ser Asn Arg Lys Tyr Pro Arg Leu Lys Asp
35 40 45

Val Asp Asp Val Leu Gly Gly Ala Ala Ala Trp Glu Asn Val Asp Ser
50 55 60

Thr Glu Glu Lys Cys Pro Lys Cys Gly His Glu Arg Ala Tyr Phe Met
65 70 75 80

Gln Ile Gln Thr Arg Ser Ala Asp Glu Pro Met Thr Thr Phe Tyr Lys
85 90 95

Cys Cys Asn Gln Leu Cys Gly His Gln Trp Arg Asp
100 105

<210> 21
<211> 1567
<212> DNA
<213> Ixodes scapularis

<220>
<221> misc_feature
<222> (785)..(785)
<223> n is a, c, g, or t

<400> 21
ccccccaggc gcagggcttc gttcaggtcg accaggggc cctccccgca agccccgagg 60

agcgccacct ggcaagcatg caggtcaatg gatatgagaa ccccacctac aagtacttcg 120

aggccaacac caactgagcg gccacgcccc caggggaggg ggaaaagggg gcggacggac 180

gtattgtgcc tgctgcgggc tgcgggatta gctcgtcccg cgttgttccg ggagccagtt 240

ggtttgcctc gcgtcttagg agtaggcacg gcctcccttc tgcacccggt caaggaccat 300

ggttgttggg gacacgagcg gcgtggggcg cagccagcct gagctttggg tcccggtacc 360

acggcaaacc gtttgttccc acccgcggaa tgaaaatttt gtttgcctca gtttctttcg 420

aatcgagcgt cggcgccgcc tccgacagcc ccgagtgcac tctgtctgtt gcgaaagacc 480

aatggagtag ttgacactcg ggtcgcagct cgaacaagct cccgtaaaac gctacttaac 540

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